



## Clinical Research

## Therapeutic evaluation of “Ayush Tulsi Jiwan Plus” oil for chronic musculoskeletal pain relief

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## Abstract

**Background:** Chronic pain of musculoskeletal origin is a very common symptom and has major effect on the physical, mental, and economic aspects of the patients. There is always a crave among physicians and patients for effective analgesic, curable preparation that can be locally applied. **Aim:** The aim of this study is to assess the efficacy and safety of “Ayush Tulsi Jiwan Plus” oil in chronic pain management of musculoskeletal origin. **Materials and Methods:** Fifty patients of chronic musculoskeletal pain of unknown origin of mild to moderate condition were advised to apply “Ayush Tulsi Jiwan Plus” oil locally twice daily for 6 weeks and examined weekly. After completion of the treatment, the efficacy of the therapy was assessed on the basis of the subjective criteria such as perception of pain, tenderness, swelling, and joint mobility. **Results:** In this study, mean baseline score versus last visit score of pain ( $2.84 \pm 0.68$  vs.  $1.33 \pm 0.76$ ), tenderness ( $1.64 \pm 0.74$  vs.  $0.36 \pm 0.56$ ), and swelling ( $0.64 \pm 0.85$  vs.  $0.38 \pm 0.66$ ) was significantly decreased, and also clinical improvement was seen in the study participants along with no evidence of adverse drug reactions. **Conclusion:** The analysis of the overall effect of this “Ayush Tulsi Jiwan Plus” oil preparation was found efficacious and topically safe in chronic pain conditions. However, further study will be required with larger sample size and in heterogeneous population to elicit long-term effect of this polyherbal preparation.

**Key words:** Ayush Tulsi Jiwan Plus, chronic musculoskeletal pain, polyherbal oil

## Introduction

Chronic musculoskeletal pain is a common symptom of the human population. It has been reported since time immemorial. The most acceptable definition of chronic pain is the pain which last for more than 3–6 months.<sup>[1,2]</sup> Another popular alternative definition of chronic pain, not required arbitrarily fixed timeline, is “pain that exerts beyond the expected period of healing.”<sup>[2]</sup> There is only a few cogent evidence for treating most types of chronic pain with opioids.<sup>[3]</sup> Opioids may improve pain for the scrimpy duration but overall improvement in functioning and its analgesic effect is doubtful with high risk of overdose and dependence.<sup>[4]</sup> In the United States alone, about 100 million people have chronic pain, in which 25 million have more or frenetic chronic pain.<sup>[3]</sup>

Chronic pain may be further subdivided into “nociceptive” and “neuropathic” pain.<sup>[5]</sup> The superficial pain is originated by activation of nociceptors in the superficial tissues or skin, and the deep somatic pain is initiated by provocation of nociceptors in blood vessels, muscles, fasciae, ligaments, tendons, and bones. The temper of the deep somatic pain is poorly localized and dull-aching. Visceral pain is the pain originating from several visceral organs when inflamed or damaged due to any etiological factors.<sup>[6]</sup> Neuralgia (neuropathic pain) is divided into “peripheral neuropathic pain” and “central neuropathic

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pain" according to its origin.<sup>[7]</sup> The type of nerve fibers that are considered to propagate the chronic pain signals are C-fibers since these carry impulse in a very tardy nature and produce painful sensation that prevails for a long time.<sup>[8]</sup> Once the process is established, it is very difficult to reverse or eradicate in case of chronic pain.<sup>[9]</sup> In some genetic variants, the interference with neuronal differentiation leads to permanent reduction in the pain threshold, which ultimately results in chronic pain.<sup>[10]</sup>

Chronic musculoskeletal pain is mainly a consequence of a complex reciprocation of biochemical, mechanical, psychological, and social components.<sup>[11]</sup> Dynamic management of chronic pain is different from that of acute musculoskeletal pain to a great extent. Insight to the pain physiology, modulation, and perception is decisive for effective management. Pharmacotherapy and nonpharmacological therapies such as psychotherapy and biofeedback practice can be used to deal chronic pain. Many evidence-based therapeutic recommendations have been formed for chronic pain conditions such as low backache, osteoarthritic, neuropathic, and posttraumatic pain. However, complete and sustained subsidence of many types of chronic pain is difficult though some can be done to improve quality of life.<sup>[9]</sup> Apart from analgesics, limitations to conventional medical management of chronic pain indicate a genuine need for novel, safe, and effective treatments for these type of patients. Now, Ayurvedic medicine has been recognized by the World Health Organization as a complete system of natural medicine, which may have the potential to provide a solution to this problem.<sup>[12]</sup> In this study, the Ayurvedic polyherbal oil treatment for chronic musculoskeletal pain has been studied for its safety and efficacy and looked for the symptomatic relief without harmful side effects. Therefore, this study was in search for effective alternative and additional therapies for chronic pain.

## Materials and Methods

Outdoor patients, having chronic pain of musculoskeletal origin (e.g., low backache, knee, shoulder, elbow, wrist, ankle, and neck pain for more than 12 weeks) fulfilling the inclusion criteria, willingly ready to give informed written consent to participate in this study and also ready to attend scheduled outpatient department visits of Department of Orthopaedics, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India, were screened for the present clinical trial. Total numbers of fifty patients were selected irrespective of sex, race, caste, religion, income, literacy, etc., However, some other data such as sociodemographic profile and relevant clinical data of participants were also recorded. The permission was taken from the Institutional Ethical Committee (No. 147-1/16/1/2015) and also registered to the Clinical Trial Registry of India (CTRI/2015/02/005523) before conducting this clinical trial.

### Inclusion criteria

- Patients of either sex aged between 25 and 65 years
- Patients with idiopathic primary backache, knee pain, and any musculoskeletal pain for more than 12 weeks.

### Exclusion criteria

- History of any trauma/fractured joint/surgical/diagnostic intervention with reference to the affected joint(s)
- Gross disability in performing daily normal routine, i.e., bed-ridden patients or confined to a wheelchair
- Patients with co-morbidities such as gouty arthritis, rheumatoid arthritis, and psoriatic arthritis
- Patients having any deformity of knee hip or back altering their gait and posture
- Patients with uncontrolled hypertension (>160/100 mm of Hg)
- Patients with uncontrolled diabetes mellitus (HbA1c >9%)
- Patients with evidence of malignancy
- Patients on prolonged (>6 weeks) medication with corticosteroids, antidepressants, anticholinergics, etc., or any other drugs that may have an influence on the outcome of the study
- Patients who have a history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke, or severe arrhythmia in the last 6 months
- Patients with any severe renal or hepatic or any other disorder which may interfere in the study
- Pregnant/lactating woman.
- Patients who are currently participating in any other clinical trial
- Any other condition which the Principal Investigator thinks may jeopardize the study.

### Study design and drug intervention

This study was an open, prospective, and time bound clinical trial, performed in a small group of population with chronic pain to assess the efficacy and safety of the interventional drug "Ayush Tulsi Jiwan Plus" oil. The amount of "Ayush Tulsi Jiwan Plus" oil used was directly proportional to the area of the joint having pain. It was advised to apply locally as few drops for small joints and up to 2–3 ml for the larger joints, twice daily for 6 weeks. The formulation and percent composition of each ingredient of this oil has been decided and prepared by the sponsor [Table 1].

The patients were examined weekly, and suitable scoring pattern and objective signs were recorded to assess any change present in the patients. The initial findings were considered as baseline score, and subsequent scores at first visit (on 1<sup>st</sup> week), second visit (on 2<sup>nd</sup> week), third visit (on 3<sup>rd</sup> week), fourth visit (on 4<sup>th</sup> week), and last visit (on 6<sup>th</sup> week) were recorded. After completion of 6 weeks of the treatment, the efficacy of the therapy was assessed on the basis of the subjective criteria as stated below.

**Table 1: Contents of "Ayush Tulsi Jiwan Plus" oil (polyherbal Ayurvedic formulation)**

Appellative	Botanical name	Percentage
Mustard oil	<i>Brassica juncea</i> (L.) Czern.	60
Turpentine oil	<i>Pinus bhutanica</i> Grierson	10
Garlic	<i>Allium sativum</i> L.	10
Ratanjot	<i>Onosma echioides</i> L.	5
Pudina Satwa	<i>Mentha longifolia</i> (L.) Huds.	5
Ajwain Satwa	<i>Trachyspermum ammi</i> Sprague.	5
Camphor	<i>Camphora officinarum</i> Baub.	5

### Perception of the pain

The slight modification was done in universally accepted, "The Faces Pain Scale" for easier assessment of pain and termed it as, "Modified Universal Pain Assessment Tool."<sup>[13]</sup>

Score	Nature of pain
5	Night pain with sleep disturbance
4	Persistent pain not able to perform daily work
3	Persistent pain can able to perform daily work
2	Persistent pain increased on exertion
1	Pain only on exertion
0	No pain

### Swelling

In the similar way, the swelling and tenderness<sup>[14]</sup> assessment tools were applied for the proper and easier clinical assessment.

Score	Nature of swelling
4	Joint swelling to a maximally abnormal degree
3	Markedly abnormal swelling
2	Joint swelling obvious even on casual observation
1	Joint swelling which may not be apparent on casual inspection, but should be recognizable to an experienced examine
0	No swelling

### Tenderness

Score	Nature of tenderness
4	Withdrawal (+ "Jump Sign") to non-noxious stimuli (i.e., superficial palpation, pinprick, and gentle percussion)
3	Tenderness with withdrawal (+ "Jump Sign")
2	Tenderness with grimace and/or flinch to palpation
1	Tenderness to palpation without grimace or flinch
0	No tenderness

### Joint mobility

The joint mobility was assessed in terms of severe restriction (about 75% loss of total joint mobility), moderate restriction (25–75% loss of total joint mobility), and mild restriction (<25% loss of total joint mobility).

### Assessment of compliance

Among the various available methods to assess the compliance, integration method was used. On each visit, information regarding the use of oil was given to the every studied participant, and all participants were advised to bring their remaining oil container and empty bottles on the next visit. The participants were also interviewed regarding the use of the oil and residual volume of oil measurement done on every visit. The consumption of  $\geq 80\%$  of prescribed oil was considered as compliance.

### Statistical analysis

The information gathered on the basis of above observations was subjected to statistical analysis. The data collected were analyzed using IBM SPSS Statistics for Windows. (Version 20.0. Armonk, NY: IBM Corp.). Continuous data were presented as mean values and standard deviation (SD) while categorical data were presented as percentages. Descriptive statistics were used

to analyze the data, and results were represented in tabular form or graphically. The repeated measures ANOVA followed by Bonferroni *post hoc* analysis was used to evaluate the efficacy of the oil, taking consideration into baseline and last visit. The level of statistical significance (*P* value) was set at 0.05.

The subjective effect was decided on the basis of individual improvement in symptoms and the assessment tools parameters.

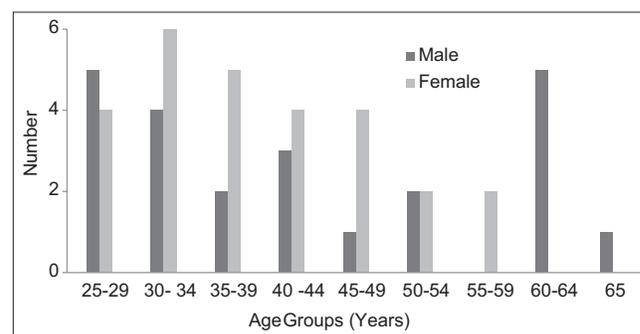
### Observations

During the study period, a total of fifty patients were selected to participate in this study. All patients willingly provided consent and participated. Female patients ( $n = 27$ , 54.00%) participated more as compared to male patients ( $n = 23$ , 46.00%) [Figure 1]. The mean age of the study population was found to be  $40.54 \pm 11.31$  years. Of 35 total study populations, overweight patients were 22 (44%) and obese patients were 13 (26%). Total 39 (78.00%) patients were under the age of 50 years, of which 20% patients were below 30 years [Figure 2]. The sociodemographic parameters of the study participants are shown in Table 2.

The clinical variables of all participants are shown in Table 3. The mean duration of pain was  $8.16 \pm 6.30$  months and 64% of participants were suffering from knee pain and low backache. The patients having chronic pain of less than a year contributed more to this study (76%). The most common site of pain was low backache (34%), which was followed by knee pain (30%) in the study population. Thirty-two percent of the participants had multiple joint pain. Sixty percent of the participants presented with limitations of joint movement, in which only two patients with severe limitation of joint movement successfully qualified the screening criteria. The hypertensive and diabetic patients participated equally in this study (30% each). There were only two patients who had previous history of allergy: One with non-steroidal anti-inflammatory drug and another one with sulfur-containing drugs.

### Results

In this study, the appreciable differences seen between the mean scores of baseline and last visit of pain, tenderness, and swelling were  $2.84 \pm 0.68$  versus  $1.33 \pm 0.76$ ,  $1.64 \pm 0.74$  versus  $0.36 \pm 0.56$ , and  $0.64 \pm 0.85$  versus  $0.38 \pm 0.66$ , respectively. The pattern of mean score of pain, tenderness, and swelling gradually decreased on subsequent visits, which graphically represents downward slope [Figures 3-5].

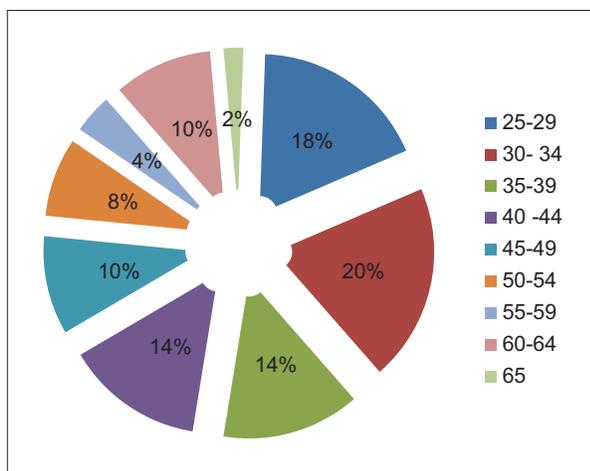


**Figure 1: Age and sex distribution of the chronic pain patients visited in outpatient department**

**Table 2: Sociodemographic parameters of study participants**

Parameters	Value (n)	Percentage
Age (years)		
Mean±SD (range)	40.54±11.31 (25-65)	
Sex		
Male	23	46.00
Female	27	54.00
Religion		
Hindu	48	84.00
Muslim	1	02.00
Christian	1	02.00
Others	0	00.00
Marital status		
Married	41	82.00
Single	7	14.00
Separated	2	04.00
Weight		
Normal/underweight	15	30.00
Overweight	22	44.00
Obese	13	26.00
Educational status		
Illiterate	0	00.00
Up to school level	14	28.00
Graduate	30	60.00
Postgraduate	4	08.00
Occupational type		
Sedentary jobs	17	34.00
Nonsedentary jobs	17	34.00
Others: homemakers, student, retired, etc.	16	32.00

SD: Standard deviation



**Figure 2: Age distribution of the study participants**

The further statistical comparison of means was done by applying repeated measures ANOVA individually for pain, tenderness, and swelling and also found that there was a significant difference between the means on subsequent visits at  $P < 0.05$  [Table 4]. Further Bonferroni *post hoc* test, was

**Table 3: Clinical variables of the study population**

Clinical variables	Frequency (n)	Percentage
Duration of chronic pain (months)		
Mean±SD (range)	8.16±6.30 (3-30)	
≤5	22	44
6-10	16	32
11-15	06	12
16-20	03	6
21-25	02	4
26-30	01	2
Sites of the pain		
Wrist	3	6
Elbow	2	4
Shoulder	5	10
Nape of the neck/upper backache	6	12
Low backache	17	34
Knee	15	30
Ankle	2	4
Pattern of joints involvement		
Single joint	34	68
Multiple joint	16	32
Joint mobility limitation		
No limitation	20	40
Mild limitation	17	34
Moderate limitation	11	22
Severe limitation	2	4
Associated comorbidities		
Diabetes	15	30
Hypertension	15	30
Cardiac illness	1	2
Dyslipidemia	2	4
BPH	2	4
Gastritis	8	16

SD: Standard deviation, BPH: Benign prostatic hyperplasia

applied for visit-wise comparisons, which showed the significant difference in pain score in all the visits except in the second and 3<sup>rd</sup> third visit [Table 5]. There was also a significant difference in tenderness score, which was found in all visits except in 4<sup>th</sup> week visit and last (6<sup>th</sup> week) visit [Table 6]. The further significant difference in means of the swelling score was seen after third visit from the baseline [Table 7]. This oil has also shown the effect on joint mobility; 15 participants out of 17 showed excellent result over limitation to joint movement [Figure 6].

During the study period, no patient had any adverse reaction associated with this polyherbal oil preparation.

## Discussion

Chronic pain has a lot of impact on our day to day life. A review of recent literature observing the neurobiology and pathophysiology of chronic pain showed that this highly prevalent condition has negative impacts on multiple aspects of

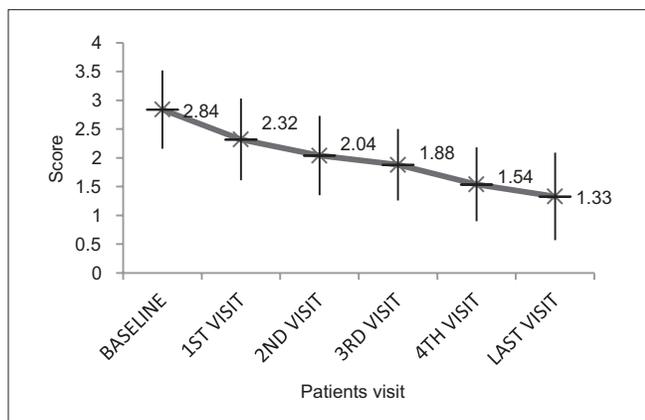


Figure 3: Effect of "Ayush Tulsi Jiwan Plus" oil over pain

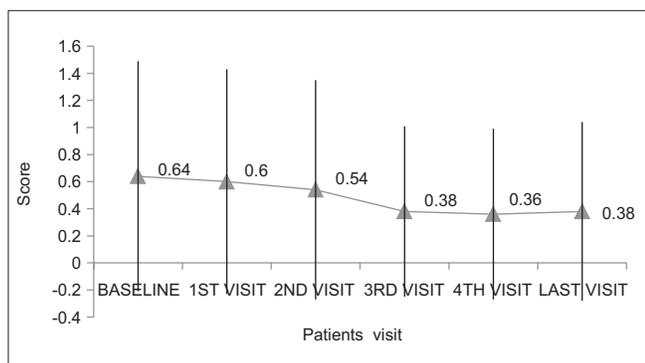


Figure 5: Effect of "Ayush Tulsi Jiwan Plus" oil over swelling

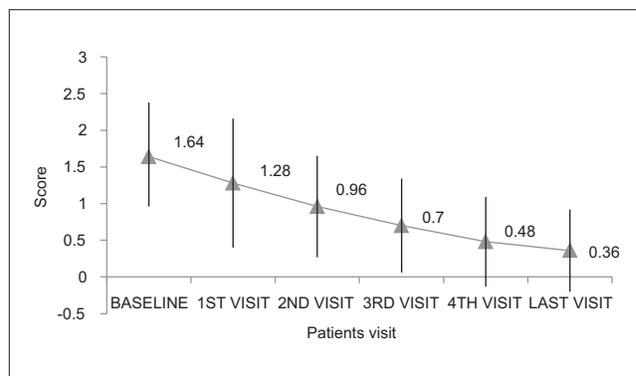


Figure 4: Effect of "Ayush Tulsi Jiwan Plus" oil over tenderness

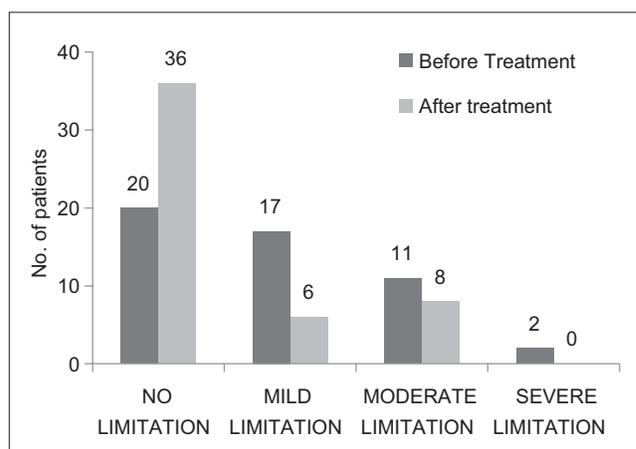


Figure 6: Effect of "Ayush Tulsi Jiwan Plus" oil on joint movement

patient health such as sleep, cognitive processes and function of brain, mood or mental health, cardiovascular wellness, sexual function, and overall quality of life. In addition, the chronic pain can become more complex in its pathophysiology, and thus, it is potentially harder to treat over time. The chronic pain can also incur significant economic consequences along with various health complications for patients.<sup>[15]</sup>

The mean  $\pm$  SD age of patients in this study was  $40.54 \pm 11.31$  years with ranges between 25 and 65 years; this may be due to the strict inclusion and exclusion criteria and small number of study participants for this clinical trial. The female patients (54.00%) participated more as compared to males; this sex distribution is comparable to the study done in the elderly where females had more prevalence of chronic pain.<sup>[15]</sup> Seventy percent of total study participants were obese or overweight, which is in accordance to the previous study.<sup>[16,17]</sup> A maximum number of patients, i.e. 78%, were under the age of 50 years, mainly due to other patients with chronic pain having other associated comorbidities or diagnosed with other autoimmune/inflammatory arthritic conditions were excluded from this study. Of fifty participants, 64% of participants were having chronic low backache and knee pain. The mean duration of pain in this study was  $8.16 \pm 6.30$  months, which may be due to small sample size. The 16 participants had more than one joint pain, among these multiple joint pain patients, most of them had the history of pain more than a year which gradually increased by the time. The other common metabolic disorders such as, diabetes (30%) and hypertension (30%) were evenly distributed in this study group.

Mustard oil (*Brassica juncea* [L.] Czern.) contains about 60% monounsaturated fatty acids (42% erucic acid and 12% oleic acid), 21% polyunsaturated fatty acids (6% the omega-3 alpha-linolenic acid and 15% the omega-6 linoleic acid), and about 12% of saturated fats.<sup>[18]</sup> Omega-3 fatty acids have potency to improve rheumatoid arthritis due as its metabolites have inhibitory role in the production of inflammatory cytokines responsible for arthritic pain and also effective against arthritic pain as well as other symptoms, including joint stiffness.<sup>[19,20]</sup> Mustard oil has stimulant and counter irritant properties and it is also mentioned in classical Ayurvedic literatures.<sup>[21]</sup> Due to these properties, it is included in "The Ayurvedic Pharmacopoeia of India".<sup>[22]</sup>

Turpentine oil (*Pinus bhutanica* Grierson), has been used since ancient times. It is counter irritant, rubefacient, inflammation and swelling resolver. Turpentine oil may cause warmth and redness which can help relieve pain in the tissues underneath. It has been considered helpful for wound healing, treating scurvy, healing of ulcers, reducing vascular inflammation and valuable in the pain of rheumatic origin.<sup>[23,24]</sup> Garlic (*Allium sativum* L.) has gained a reputation in various traditions as a prophylactic as well as therapeutic medicinal plant. It has played important dietary and medicinal roles throughout the history. Garlic has anti-inflammatory activity<sup>[25]</sup> and antibacterial property.<sup>[26-28]</sup>

Traditionally, almost all parts of *Ratanjot* (*Onosma echioides* L.) plants have medicinal properties.<sup>[29]</sup> Plants are used as a stimulant in bladder pain, palpitation of heart, kidney irritation, and

**Table 4: Repeated measures ANOVA of "Ayush Tulsi Jiwan Plus" oil (Tests of Within-Subjects Effects)**

Source	Type III Sum of Squares	df	Mean Square	F
<b>PAIN</b>				
Duration				
Sphericity Assumed	47.509	5	9.502	66.991***
Greenhouse-Geisser	47.509	3.439	13.815	66.991***
Huynh-Feldt	47.509	5.000	9.502	66.991***
Lower-bound	47.509	1.000	47.509	66.991***
Error (Duration)				
Sphericity Assumed	24.821	175	0.142	
Greenhouse-Geisser	24.821	120.359	0.206	
Huynh-Feldt	24.821	175.000	0.142	
Lower-bound	24.821	35.000	0.709	
<b>TENDERNESS</b>				
Duration				
Sphericity Assumed	43.543	5	8.709	48.002***
Greenhouse-Geisser	43.543	3.758	11.586	48.002***
Huynh-Feldt	43.543	5.000	8.709	48.002***
Lower-bound	43.543	1.000	43.543	48.002***
Error (Duration)				
Sphericity Assumed	31.749	175	0.181	
Greenhouse-Geisser	31.749	131.538	0.241	
Huynh-Feldt	31.749	175.000	0.181	
Lower-bound	31.749	35.000	0.907	
<b>SWELLING</b>				
Duration				
Sphericity Assumed	3.613	5	0.723	10.587***
Greenhouse-Geisser	3.613	1.906	1.895	10.587***
Huynh-Feldt	3.613	2.820	1.281	10.587***
Lower-bound	3.613	1.000	3.613	10.587**
Error (Duration)				
Sphericity Assumed	11.946	175	0.068	
Greenhouse-Geisser	11.946	66.721	0.179	
Huynh-Feldt	11.946	98.692	0.121	
Lower-bound	11.946	35.000	0.341	

df: Degree of Freedom, F: Variance of the group means/mean of the within group variance, Significant F as per critical F value (\* $\leq 0.05$ , \*\* $\leq 0.01$ , and \*\*\* $\leq 0.001$ )

rheumatism<sup>[30]</sup> while roots have cooling, astringent, demulcent, and diuretic action. *O. echioides* has various medicinal properties such as anti-inflammatory, antipyretic, analgesic, antiseptic, cardiac tonic, and wound healing. It is also used in skin disease.<sup>[31-36]</sup>

Numerous studies on *Pudina Satwa* (*Mentha longifolia* [L.] Huds.) have shown various pharmacological and therapeutic effects of the plant.<sup>[37,38]</sup> *M. longifolia* has significant antimicrobial activities,<sup>[39,40]</sup> antinociceptive, antipyretic, antiemetic, antispasmodic, and carminative.<sup>[41-43]</sup> It has also central nervous system stimulant and antioxidant properties.<sup>[40]</sup>

*Ajwain Satwa* (*Trachyspermum ammi* Sprague.), with its characteristic aromatic smell and pungent taste, is widely used as a spice in curries. It has been shown to possess digestive stimulant,<sup>[44]</sup> hypolipidemic,<sup>[45]</sup> anti-inflammatory,<sup>[46]</sup> antimicrobial,<sup>[47]</sup> anthelmintic,<sup>[48]</sup> bronchodilating, antihypertensive, hepatoprotective, antispasmodic,<sup>[49]</sup> antilithiasis, diuretic,<sup>[50]</sup> abortifacient,<sup>[51]</sup> galactogogic,<sup>[52]</sup> antiplatelet-aggregatory,<sup>[53]</sup>

antitussive,<sup>[54]</sup> antifilarial,<sup>[55]</sup> gastroprotective,<sup>[56]</sup> nematocidal,<sup>[57]</sup> anthelmintic,<sup>[48]</sup> detoxification of aflatoxins,<sup>[58]</sup> and ameliorative effects.<sup>[59]</sup>

Camphor (*Camphora officinarum* Baub.) has long been prescribed in traditional medicine for the treatment of inflammatory diseases such as musculoskeletal pains, rheumatic condition, sprains, and bronchitis. *C. officinarum* has anti-inflammatory mechanisms blocked the production of interleukin-1, interleukin-6, and tumor necrosis factor- $\alpha$  from RAW264.7 cells and nitrous oxide, prostaglandin E2 production in lipopolysaccharide or interferon- $\gamma$ -activated macrophages.<sup>[60]</sup> Camphor has also diaphoretic action with mild analgesic properties.<sup>[61,62]</sup>

In view of anti-inflammatory, antiseptic, and analgesic properties of each ingredient, hypothesis was made that this novel Ayurvedic combination can have synergistic effect over chronic pain. Hence, clinical trial was conducted to observe the efficacy and safety of this polyherbal preparation.

**Table 5: Bonferroni post hoc test (visit-wise comparisons over pain)**

Visit	Time	Mean difference	SE	95% CI for difference <sup>a</sup>	
				Lower bound	Upper bound
Baseline	First visit	0.520***	0.071	0.300	0.740
	Second visit	0.800***	0.057	0.624	0.976
	Third visit	0.960***	0.075	0.727	1.193
	Fourth visit	1.300***	0.077	1.063	1.537
	Last visit	1.540***	0.091	1.258	1.822
First visit	Baseline	-0.520***	0.071	-0.740	-0.300
	Second visit	0.280**	0.070	0.063	0.497
	Third visit	0.440***	0.086	0.173	0.707
	Fourth visit	0.780***	0.082	0.526	1.034
	Last visit	1.020***	0.093	0.734	1.306
Second visit	Baseline	-0.800***	0.057	-0.976	-0.624
	First visit	-0.280**	0.070	-0.497	-0.063
	Third visit	0.160	0.072	-0.062	0.382
	Fourth visit	0.500***	0.071	0.280	0.720
	Last visit	0.740***	0.080	0.494	0.986
Third visit	Baseline	-0.960***	0.075	-1.193	-0.727
	First visit	-0.440***	0.086	-0.707	-0.173
	Second visit	-0.160	0.072	-0.382	0.062
	Fourth visit	0.340***	0.068	0.131	0.549
	Last visit	0.580***	0.076	0.345	0.815
Fourth visit	Baseline	-1.300***	0.077	-1.537	-1.063
	First visit	-0.780***	0.082	-1.034	-0.526
	Second visit	-0.500***	0.071	-0.720	-0.280
	Third visit	-0.340***	0.068	-0.549	-0.131
	Last visit	0.240**	0.061	0.052	0.428
Last visit	Baseline	-1.540***	0.091	-1.822	-1.258
	First visit	-1.020***	0.093	-1.306	-0.734
	Second visit	-0.740***	0.080	-0.986	-0.494
	Third visit	-0.580***	0.076	-0.815	-0.345
	Fourth visit	-0.240**	0.061	-0.428	-0.052

\*The mean difference is significant at the P value 0.05 level (\*≤0.05, \*\*≤0.01, and \*\*\*≤0.001). CI: Confidence interval, SE: Standard error

In this study, mean baseline parameters versus last visit (i.e., 6<sup>th</sup> week) parameters of pain ( $2.84 \pm 0.68$  vs.  $1.33 \pm 0.76$ ), tenderness ( $1.64 \pm 0.74$  vs.  $0.36 \pm 0.56$ ), and swelling ( $0.64 \pm 0.85$  vs.  $0.38 \pm 0.66$ ) were statistically decreased significantly, and also clinical improvement was seen in the study participants. The gradual downward slope of the means was observed due to gradual decrease in the mean score of pain, tenderness, and swelling, which suggests the efficacy of "Ayush Tulsi Jiwan Plus" oil, and decreasing trend of graphical representations of these parameters showed gradual improvements in subsequent follow-ups.

The effect of "Ayush Tulsi Jiwan Plus" polyherbal topical oil preparation has shown significance difference between its means in detailed statistical analysis. The means of pain score in all the visits were significantly decreased except in between the second and third visits. Significant difference in tenderness score was found in all visits except in 4<sup>th</sup> week visit

**Table 6: Bonferroni post hoc test (visit-wise comparisons over tenderness)**

Visit	Time	Mean difference	SE	95% CI for difference <sup>a</sup>	
				Lower bound	Upper bound
Baseline	First visit	0.360***	0.074	0.131	0.589
	Second visit	0.680***	0.078	0.440	0.920
	Third visit	0.940***	0.060	0.755	1.125
	Fourth visit	1.160***	0.083	0.905	1.415
	Last visit	1.280***	0.095	0.987	1.573
First visit	Baseline	-0.360***	0.074	-0.589	-0.131
	Second visit	0.320**	0.078	0.080	0.560
	Third visit	0.580***	0.086	0.314	0.846
	Fourth visit	0.800***	0.095	0.508	1.092
	Last visit	0.920***	0.102	0.604	1.236
Second visit	Baseline	-0.680***	0.078	-0.920	-0.440
	First visit	-0.320**	0.078	-0.560	-0.080
	Third visit	0.260*	0.080	0.014	0.506
	Fourth visit	0.480***	0.091	0.198	0.762
	Last visit	0.600***	0.090	0.321	0.879
Third visit	Baseline	-0.940***	0.060	-1.125	-0.755
	First visit	-0.580***	0.086	-0.846	-0.314
	Second visit	-0.260*	0.080	-0.506	-0.014
	Fourth visit	0.220*	0.066	0.017	0.423
	Last visit	0.340***	0.079	0.097	0.583
Fourth visit	Baseline	-1.160***	0.083	-1.415	-0.905
	First visit	-0.800***	0.095	-1.092	-0.508
	Second visit	-0.480***	0.091	-0.762	-0.198
	Third visit	-0.220*	0.066	-0.423	-0.017
	Last visit	0.120	0.068	-0.089	0.329
Last visit	Baseline	-1.280***	0.095	-1.573	-0.987
	First visit	-0.920***	0.102	-1.236	-0.604
	Second visit	-0.600***	0.090	-0.879	-0.321
	Third visit	-0.340***	0.079	-0.583	-0.097
	Fourth visit	-0.120	0.068	-0.329	0.089

\*The mean difference is significant at the P value 0.05 level (\*≤0.05, \*\*≤0.01, and \*\*\*≤0.001). CI: Confidence interval, SE: Standard error

and last (6<sup>th</sup> week) visit. The oil effect in swelling has been seen after 3 weeks of therapy as significant difference in means of the swelling score was seen only after third visit from the baseline. After application of this oil, a significant number of patients with decreased joint mobility were also improved. This may be due to the combined effect of decrease in pain, tenderness, and swelling, which contributed to improvement of joint condition and its mobility.

In the present study, only fifty patients (aged between 25 and 65 years) of chronic pain of unknown origin, those were in mild

**Table 7: Bonferroni post hoc test (visit-wise comparisons over swelling)**

Visit	Time	Mean difference	SE	95% CI for difference <sup>a</sup>	
				Lower bound	Upper bound
Baseline	First visit	0.040	0.040	-0.083	0.163
	Second visit	0.100	0.052	-0.059	0.259
	Third visit	0.260**	0.069	0.047	0.473
	Fourth visit	0.280**	0.070	0.063	0.497
	Last visit	0.260*	0.075	0.030	0.490
First visit	Baseline	-0.040	0.040	-0.163	0.083
	Second visit	0.060	0.034	-0.045	0.165
	Third visit	0.220**	0.059	0.037	0.403
	Fourth visit	0.240**	0.061	0.052	0.428
	Last visit	0.220*	0.066	0.017	0.423
Second visit	Baseline	-0.100	0.052	-0.259	0.059
	First visit	-0.060	0.034	-0.165	0.045
	Third visit	0.160	0.052	-0.002	0.322
	Fourth visit	0.180*	0.055	0.011	0.349
	Last visit	0.160	0.060	-0.024	0.344
Third visit	Baseline	-0.260**	0.069	-0.473	-0.047
	First visit	-0.220**	0.059	-0.403	-0.037
	Second visit	-0.160	0.052	-0.322	0.002
	Fourth visit	0.020	0.020	-0.042	0.082
	Last visit	0.000	0.029	-0.088	0.088
Fourth visit	Baseline	-0.280**	0.070	-0.497	-0.063
	First visit	-0.240**	0.061	-0.428	-0.052
	Second visit	-0.180*	0.055	-0.349	-0.011
	Third visit	-0.020	0.020	-0.082	0.042
	Last visit	-0.020	0.020	-0.082	0.042
Last visit	Baseline	-0.260*	0.075	-0.490	-0.030
	First visit	-0.220*	0.066	-0.423	-0.017
	Second visit	-0.160	0.060	-0.344	0.024
	Third visit	0.000	0.029	-0.088	0.088
	Fourth visit	0.020	0.020	-0.042	0.082

\*The mean difference is significant at the P value 0.05 level (\* $\leq$ 0.05, \*\* $\leq$ 0.01, and \*\*\* $\leq$ 0.001). CI: Confidence interval, SE: Standard error

to moderate pain condition, were selected. Hence, further study will be required with larger sample size and in heterogeneous population. Regarding the efficacy of "Ayush Tulsi Jiwan Plus" oil, it was found effective for chronic pain of musculoskeletal origin and showed continuous reduction of pain, tenderness, and swelling and improvement of joint mobility with clinically significant results seen within 45 days of treatment. In view of zero evidence of major or minor adverse drug reaction, it is considered being safe as topical application.

## Conclusion

Concisely, this clinical study, which investigated the effects of "Ayush Tulsi Jiwan Plus" Oil on patients who were suffering from chronic pain of musculoskeletal origin, showed that this polyherbal topical preparation was effective in reducing patient's subjective pain, tenderness, and swelling along with

improvement in joint mobility. These results suggest that the local application of "Ayush Tulsi Jiwan Plus" oil might be a valuable polyherbal preparation for chronic pain relief of musculoskeletal origin.

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## Conflicts of interest

There are no conflicts of interest.

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## हिन्दी सारांश

# तुलसी जीवन प्लस तैल का सिरकालिन मांसपेशी शूल में प्रभाव का एक प्रयोगात्मक अध्ययन

कुणाल शर्मा, दीप सुन्दर साहु, अबिचल चटोपाध्याय, जगन्नाथ साहु, संजय कुमार, शुधांशु शेखर मिश्रा

मांसपेशी में पुरातन शूल होना यह एक बहु प्रचलित लक्षण है, और, इससे ज्यादातर रोगियों के सार्वदैहिक, मानसिक एवं आर्थिक स्थिती पर प्रभाव होता है। रोगियों एवं चिकित्सको द्वारा सर्वदा इस शूलहरण के लिये एक उचित उपाय खोजने का प्रयास रहता है। तुलसी जीवन प्लस, यह बहुत सारे जड़ी बूटियों से निर्मित एक आयुर्वेद, है, इसका मिलित रूप से मांसपेशी का शूल में असर और पार्श्वप्रतिक्रिया देखने के लिए किया गया। पुराने शूल से ग्रस्त होने वाले ५० रोगियों जिसकी, उम्र जैसे २५ से ७५ किये गये, और के थी, इंस्टिट्यूट ऑफ मेडिकल साइंस, सोम अस्पताल के बहिरंग विभाग से चुने गये। में तुलसी जीवन तैल का पुरातन शूल में असर देखा गया। ४५ दिन तक, दिन में २ बार मालिश करने के लिए दिया गया। अध्ययन पूर्व और अध्ययन के पश्चात सारे लक्षणों को लिपिबद्ध किया गया। संपूर्ण अवधि के बाद यह देखा गया कि रोगियों का सार्वदैहिक विकृतियों के अंतर्गत शूल में (२.८४±०.६८) से घटकर (१.३३±०.७६), स्पर्शअसहिष्णुता में (१.६४±०.७४) से घटकर (०.३६±०.५६), सूजन में (०.६४±०.८५) घटकर (०.३८±०.६६) हो गया।, परीसंज्ञान के अनुसार यह अध्ययन महत्वपूर्ण माना जा सकता है। यह निष्कर्ष किया जा सकता है कि अवधि ४५ दिन से लेकर या इससे अधिक माह तक तथा साथ में अधिक संख्यक रोगियों में अगर अध्ययन किया जाए तो अधिक और असरदार होने की अवधि, संभावना है अध्ययन के दौरान रोगियों में कोई भी भैषज्य प्रतिकूलता हुई। प्राप्त नहीं हुआ।